

CLAIMS

1. An inhibitor of C5a activity for use in the treatment of a medical condition caused by or associated with infection with a corona virus, wherein the medical condition is preferably
5 (i) pneumonia, and/or (ii) fever.
2. An inhibitor of C5a activity for use in the reduction of an inflammatory response in a subject suffering from a corona virus infection.
- 10 3. An inhibitor of C5a activity for use in the improvement of organ function, in particular lung function and/or hepatic function, in a subject suffering from a corona virus infection.
4. The inhibitor of C5a activity for use according to any one of claims 1 to 3, wherein the corona virus is selected from the group comprising SARS-CoV, MERS-CoV and SARS-
15 CoV-2.
5. The inhibitor of C5a for use according to any one of the preceding claims, wherein the subject suffers from SARS, MERS or COVID-19.
- 20 6. The inhibitor of C5a for use according to any one of the preceding claims, wherein the treatment results in one or more of the following:
 - reduction of C-reactive protein;
 - reduction of fever;
 - increase of lymphocyte counts in blood;
 - 25 - reducing ALT/AST; and/or
 - increase of oxygen index ($\text{PaO}_2/\text{FiO}_2$).
7. The inhibitor for use according to any one of the preceding claims, wherein the inhibitor of C5a activity:
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 - lowers the concentration of C5;
 - inhibits cleavage of C5 into C5a and C5b;
 - lowers the concentration of C5a;
 - inhibits binding between C5a and a C5a receptor;
 - lowers the concentration of a C5a receptor; and/or
 - 35 - inhibits the activity of a C5a receptor.

8. The compound for use according to any one of the preceding claims, wherein the inhibitor of C5a activity is a protein ligand that specifically binds to C5, or to C5a, or to a C5a receptor.
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9. The inhibitor of C5a activity for use according to any one of the preceding claims, wherein the protein ligand is selected from the group consisting of
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- (i) antibodies or antigen-binding fragments thereof,
 - (iii) antibody-like proteins,
 - (iv) inhibitory variants of C5a,
 - (v) inhibitory variants of a C5a receptor,
 - (vi) proteins acting on the complement pathway; and
 - (vii) peptides.
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10. The compound for use according to any one of the preceding claims, wherein the inhibitor of C5a activity is an oligonucleotide that specifically binds to C5, or to C5a, or to a C5a receptor.
11. The compound for use of claim 10, wherein the oligonucleotide is selected from the group consisting of DNA-aptamers, D-RNA aptamers, and L-RNA aptamers.
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12. The compound for use according to any one of the preceding claims, wherein the inhibitor of C5a activity reduces expression of C5 protein or a C5a receptor protein.
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13. The compound for use of claim 12, wherein said inhibitor of C5a activity is an oligonucleotide selected from the group consisting of antisense DNA, antisense RNA, siRNA, and miRNA.
14. The compound for use of any one of claims 7 to 13, wherein the C5a receptor is C5aR and/or C5L2.
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15. The compound for use of any one of claims 1 to 14, wherein the inhibitor of C5a activity is selected from the group consisting of:
- (a) MEDI-7814, ALXN-1007, or NOX-D21, or an antigen-binding fragment thereof;

- (b) an antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof competes with one of the antibodies indicated under (a) for binding to C5a;
- (c) Eculizumab, ALXN1210, ALXN5500, or LFG316, or an antigen-binding fragment thereof;
- (d) an antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof competes with one of the antibodies indicated under (c) for binding to C5;
- (e) Coversin or RA101495;
- (f) an antibody or an antigen-binding fragment thereof or a protein or a macrocyclic peptide wherein said antibody or antigen-binding fragment thereof or protein or macrocyclic peptide competes with one of the proteins or peptides indicated under (e) for binding to C5;
- (g) Zimura;
- (h) an antibody or an antigen-binding fragment thereof or an aptamer, wherein said antibody or antigen-binding fragment thereof or aptamer competes with Zimura for binding to C5;
- (i) AMY-201 or Mirococept;
- (j) an antibody or an antigen-binding fragment thereof or a protein wherein said antibody or antigen-binding fragment thereof or protein competes with one of the proteins indicated under (i) for binding to C3b;
- (k) Bikaciomab;
- (l) an antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof competes with Bikaciomab for binding to Factor B;
- (m) Lampalizumab;
- (n) an antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof competes with Lampalizumab for binding to Factor D;
- (o) ALN-CC5;
- (p) Avacopan or a compound according to formula II or formula III; or PMX-53 or a compound according to formula IV;
- (q) an antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof competes with avacopan or PMX-53 for binding to C5aR;
- (r) clone S5/1 or clone 7H110, or an antigen-binding fragment thereof; and

- (s) an antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof competes with one of the antibodies indicated under (r) for binding to C5aR.
- 5 16. The inhibitor of C5a for use according to any of claims 1 to 9, wherein said inhibitor of C5a specifically binds to a conformational epitope formed by amino acid sequences NDETCEQRA (SEQ ID NO: 2) and SHKDMQL (SEQ ID NO: 3) of human C5a, and wherein the inhibitor of C5a binds to at least one amino acid within the amino acid sequence according to SEQ ID NO: 2 and to at least one amino acid within the amino acid sequence according to SEQ ID NO: 3.
- 10 17. The inhibitor of C5a for use according to any of claims 1 to 9 or 16, wherein said inhibitor of C5a is an antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof comprises
- 15 (i) a heavy chain CDR3 sequence as set forth in SEQ ID NO: 6; or
(ii) a heavy chain CDR3 sequence as set forth in SEQ ID NO: 7;
wherein the heavy chain CDR3 sequence optionally comprises 1, 2, or 3 amino acid exchanges, preferably conservative amino acid exchanges, 1, 2, or 3 amino acid deletions, and/or 1, 2, or 3 amino acid additions.
- 20 18. The inhibitor of C5a for use according to any of claims 1 to 9, 16 or 17, wherein said binding moiety is an antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof comprises
- 25 (iii) a light chain CDR3 sequence as set forth in SEQ ID NO: 8; or
(iv) a light chain CDR3 sequence as set forth in SEQ ID NO: 9;
wherein the light chain CDR3 sequence optionally comprises 1, 2, or 3 amino acid exchanges, preferably conservative amino acid exchanges, 1, 2, or 3 amino acid deletions, and/or 1, 2, or 3 amino acid additions.
- 30 19. The inhibitor of C5a for use according to any of claims 1 to 9, or 16 to 18, wherein said binding moiety is an antibody or an antigen-binding fragment thereof, wherein said antibody or antigen-binding fragment thereof comprises at least one of the following sequences:
- 35 (v) a heavy chain CDR2 sequence according to SEQ ID NO: 10;
(vi) a heavy chain CDR2 sequence according to SEQ ID NO: 11;

- (vii) a light chain CDR2 sequence according to SEQ ID NO: 12;
(viii) a light chain CDR2 sequence according to SEQ ID NO: 13;
(ix) a heavy chain CDR1 sequence according to SEQ ID NO: 14;
(x) a heavy chain CDR1 sequence according to SEQ ID NO: 15;
5 (xi) a light chain CDR1 sequence according to SEQ ID NO: 16; or
(xii) a light chain CDR1 sequence according to SEQ ID NO: 17;
wherein the heavy chain CDR2 sequence optionally comprises 1, 2, or 3 amino acid exchanges, preferably conservative amino acid exchanges, 1, 2, or 3 amino acid deletions, and/or 1, 2, or 3 amino acid additions;
10 wherein the light chain CDR2 sequence optionally comprises 1, 2, or 3 amino acid exchanges, preferably conservative amino acid exchanges, 1, 2, or 3 amino acid deletions, and/or 1, 2, or 3 amino acid additions;
wherein the heavy chain CDR1 sequence optionally comprises 1, 2, or 3 amino acid exchanges, preferably conservative amino acid exchanges, 1, 2, or 3 amino acid deletions, and/or 1, 2, or 3 amino acid additions; and
15 wherein the light chain CDR1 sequence optionally comprises 1, 2, or 3 amino acid exchanges, preferably conservative amino acid exchanges, 1, 2, or 3 amino acid deletions, and/or 1, 2, or 3 amino acid additions.
- 20 20. The inhibitor of C5a for use according to any of claims 16 to 19, wherein said binding moiety is an antibody or an antigen-binding fragment thereof, comprising
- (i) a variable heavy chain with the amino acid sequence according to SEQ ID NO: 34 and a variable light chain sequence with the amino acid sequence according to SEQ ID NO: 35 or variants with at least 90% amino acid sequence identity with SEQ ID NO: 34 and 35
25 which comprise the amino acid sequences according SEQ ID NO: 6, 8, 10, 12, 14 and 16 of the light and heavy chain CDR1 to CDR3 or variants thereof as specified in claims 15 to 18;
- (ii) a variable heavy chain sequence with the amino acid sequence of SEQ ID NO: 36 and the variable light chain sequence with the amino acid sequence according to SEQ ID NO: 37
30 or variants with at least 90% amino acid sequence identity with SEQ ID NO: 36 and 37 which comprise the amino acid sequences according SEQ ID NO: 7, 9, 11, 13, 15 and 17 of the light and heavy chain CDR1 to CDR3 or variants thereof as specified in claims 15 to 18.